General

Guideline Title

Bortezomib for induction therapy in multiple myeloma before high-dose chemotherapy and autologous stem cell transplantation.

Bibliographic Source(s)

National Institute for Health and Care Excellence. Bortezomib for induction therapy in multiple myeloma before high-dose chemotherapy and autologous stem cell transplantation. London (UK): National Institute for Health and Care Excellence; 2014 Apr. 57 p. (Technology appraisal guidance; no. 311).

Guideline Status

This is the current release of the guideline.

Recommendations

Major Recommendations

Bortezomib is recommended as an option within its marketing authorisation, that is, in combination with dexamethasone, or with dexamethasone and thalidomide, for the induction treatment of adults with previously untreated multiple myeloma, who are eligible for high-dose chemotherapy with haematopoietic stem cell transplantation.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Multiple myeloma

Guideline Category

Assessment of Therapeutic Effectiveness

Treatment

Clinical Specialty

Hematology

Oncology

Intended Users

Advanced Practice Nurses

Physician Assistants

Physicians

Guideline Objective(s)

To assess the clinical effectiveness and cost-effectiveness of bortezomib for induction therapy in multiple myeloma before high-dose chemotherapy and autologous stem cell transplantation

Target Population

Adults with previously untreated multiple myeloma who are eligible for high-dose chemotherapy with haematopoietic stem cell transplantation

Interventions and Practices Considered

Bortezomib

Major Outcomes Considered

- Clinical effectiveness
  - Response rates (complete response [CR], near CR [nCR], very good partial response [VGPR], partial response [PR], progressive disease, overall response rate)
  - Progression-free survival (PFS)
  - Time to progression
  - Overall survival (OS)
  - Proportion of patients who had stem cell transplantation
  - Adverse events
- Cost-effectiveness

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Care Excellence (NICE) commissioned an independent academic centre to perform an assessment of the manufacturer's submission on the technology considered in this appraisal and prepare an Evidence Review Group (ERG) report. The ERG report for this technology appraisal was prepared by Southampton Health Technology Assessments Centre (SHTAC) (see the "Availability of Companion Documents" field). See the Section B of the manufacturer's submission (see the "Availability of Companion Documents" field) for details on search strategies.

Clinical Effectiveness

Critique of Manufacturer's Approach to Systematic Review

Description of Manufacturer's Search Strategy

The search strategies and database selection, covering clinical, cost-effectiveness and quality of life are well documented and considered fit for purpose. A mix of index terms and free text have been applied and appropriately combined into sets, and suitable search filters were employed. All searches are reproducible and although the return of numbers on each search line is not documented, the total return is summarised in a flow chart. It is noted that exact replication of the clinical searches by the ERG would not be feasible on account of the use of different database hosts, however the strategy and syntax based on ERG searching expertise appears adequate. The re-submission of the manufacturer's submission (MS) did not affect the content of the cost search strategies as they were not drug specific.

It was not considered necessary to replicate all the searches as they appeared to be sensitive and designed for maximum recall. The ERG undertook update searches for 2012/2013, as the search undertaken by the manufacturer was September 2012 with the submission being received in February 2013. These results were screened by an ERG reviewer and no additional relevant trials were identified.

A bibliographic search of identified references has been undertaken and in-house manufacturer clinical study reports (CSRs) have been used in the submission. Key conferences relevant to the therapeutic area are recorded as having been searched, although the American Society of Haematology (ASH) 2012 conference was reported as not available at the time of the manufacturer's submission. This was searched by the ERG; no relevant abstracts were identified.

Statement of the Inclusion/Exclusion Criteria Used in the Study Selection

The MS clearly states the inclusion and exclusion criteria. The criteria deviate from the decision problem with regard to patient population, intervention and comparator. The criteria state that the patient population should include patients with multiple myeloma (MM), including symptomatic MM but do not stipulate that these should be newly diagnosed, treatment naïve patients eligible for high-dose chemotherapy and autologous stem cell transplantation (HDT-ASCT). However, they have commented that the patient population was restricted to that stated in the decision problem which is in line with the final scope.

The inclusion criteria state that the intervention may be given as monotherapy and that inclusion was not restricted to the licensed dose. These are not in line with the decision problem, the final scope nor the anticipated license which is for bortezomib combination therapy at a specific dose and for a specific number of cycles depending on the combination regimen. The MS specified there was no exclusion on the basis of comparator and that the main comparator was cyclophosphamide, thalidomide, dexamethasone (CTD) (current standard treatment in the UK) but also included studies that involved induction regimens not containing thalidomide in order to contribute to a mixed treatment comparison (MTC) analysis. This does not reflect the final scope which stipulates combination regimens containing thalidomide as the comparator. The inclusion criteria for outcomes were also broader than the decision problem and final scope in that no outcomes were specified.

Study quality and setting were not stated as inclusion or exclusion criteria, and this reflects the final scope. No limits were placed on the quality of randomised controlled trials (RCTs) and it is stated that RCTs were included regardless of blinding. Non-RCTs were included in the event that an insufficient number of relevant RCTs were found. In the non-RCT inclusion criteria, study design limitations were that non-RCTs reported as conference abstracts with a sample size ≤30, or that did not assess safety or efficacy, were excluded. Retrospective studies, case reports, case series, hospital records/database analyses, pharmacokinetic studies and phase 1 studies were also excluded (the MS reports that these studies are at higher risk of bias compared to other study designs), and the ERG agrees that it is reasonable to exclude these studies.

The MS includes a flow diagram that shows the number of publications identified through searches and the number of publications included and excluded at each stage of the review process. Reasons (and corresponding numbers) for excluding studies at the abstract and full publication review stages, are given in the diagram. In the last box in the diagram, the MS reports a total of 53 studies including 15 RCTs. Clarification requested from the manufacturer by the ERG confirmed that the remaining 38 studies were excluded as they were non-RCTs. A list of the non-RCTs identified were reported in an appendix. The MS excluded non-comparative studies at screening due to issues with bias (see previous

comment above). A critical appraisal of the included studies was presented and in a summary table, with further details in the separate appendices document of the MS.

Economic Evaluation

Manufacturer's Review of Published Economic Evaluations

A systematic search of the literature was conducted by the manufacturer to identify economic evaluations (and burden of illness studies) of treatments of newly diagnosed MM.

The inclusion criteria state that full economic evaluations, budget impact analyses and resource use studies would be included for treatment with bortezomib, thalidomide, vincristine, cyclosphosphamide and lenalidomide for first line induction therapy prior to SCT for patients with multiple myeloma. Studies were included for the time period from 2000 to November 2012 for full articles only. Only English language studies were included. From 287 titles and abstracts screened, seventeen potential studies were identified for full paper screening: and 3 studies were included for full review. Fourteen studies were excluded, mainly for the following reasons: the cost of treatment was not specified (n=5), the intervention was not relevant to this submission (n=2), or the study was not specific to patients who received transplant (n=1). The checklist suggested by NICE has been applied to the included references. The MS does not discuss the studies identified. The ERG notes that none of the studies identified are within the NICE scope for this appraisal.

Number of Source Documents

Clinical Effectiveness

The manufacturer's submission (MS) identified 15 randomised controlled trials (RCTs), of which a further six were excluded for not containing bortezomib, along with another four where both treatment arms contained bortezomib. Five RCTs were included that the MS states are relevant to the decision problem. However, the Evidence Review Group (ERG) note that only two of these (Pethema and Gimema) compare a bortezomib regimen versus a thalidomide regimen as per the decision problem and National Institute for Health and Care Excellence (NICE) final scope.

Cost-effectiveness

3 studies were included for full review.

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus

Rating Scheme for the Strength of the Evidence

Not applicable

Methods Used to Analyze the Evidence

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Care Excellence (NICE) commissioned an independent academic centre to perform an assessment of the manufacturer's submission on the technology considered in this appraisal and prepare an Evidence Review Group (ERG) report. The ERG report for this technology appraisal was prepared by Southampton Health Technology Assessments Centre (SHTAC) (see the "Availability of Companion Documents" field).

Clinical Effectiveness

Critique of the Manufacturer's Approach to Systematic Review

Description and Critique of the Approach to Validity Assessment

The manufacturer's submission (MS) provides a summary of the quality assessment of each of the five included trials with a more detailed assessment in MS Appendix 3. The quality assessment in the MS follows the NICE criteria and is appropriate. The ERG carried out an independent quality assessment of the five trials included in the review. The ERG presents the quality assessment for the Pethema and Gimema trials in Table 2 of the ERG report as these trials matched the NICE scope, whilst the assessment for the Hovon, Intergroupe Francophone du Myelome (IFM) and Medical Research Council Multiple Myeloma IX (MRC MMIX) trials is presented in Appendix 1 of the of the ERG report. As Table 2 in the ERG report shows, the ERG and the manufacturer's quality assessments of the Pethema and Gimema trials agree in part. The ERG assessment differed to that of the manufacturer on the criteria of adequate allocation concealment, group similarity at baseline and whether adequate intention-to-treat (ITT) analyses had been used.

Description and Critique of the Manufacturer's Approach to the Evidence Synthesis

The MS provides a narrative synthesis of the findings of Pethema and Gimema (the two trials that meet the scope of the appraisal) and also three studies outside the scope (Hovon, IFM, MRC MMIX), one of which does not include bortezomib (MRC MMIX).

A meta-analysis of the four bortezomib-based trials (Pethema, Gimema, Hovon and IFM) is not provided. The manufacturer states that this is because the trials are not comparable in terms of intervention regimens, the variable duration of induction, comparator arms and study design. The ERG agrees with this decision. This also holds for the two studies that meet the scope of the review (Pethema and Gimema).

As no trials comparing bortezomib-based regimens with cyclophosphamide, thalidomide and dexamethasone (CTD) (the current United Kingdom [UK] standard) were identified, the MS presents a mixed treatment comparison (MTC) in order to rank all bortezomib-based regimens and CTD.

The justification for conducting an MTC is given which is appropriate (i.e., no head-to-head trials of bortezomib-containing regimens against CTD, the regimen most commonly used in the UK). However, to be included in an MTC, trials are required to be homogeneous enough to allow pooling which is the same assumption as required for a standard pairwise meta-analysis. Therefore there is inconsistency in the MS as no standard pairwise meta-analysis is presented for reasons of heterogeneity between trials. The ERG feels that the similarity assumption for an MTC is not met due to the differences in trial designs and effect modifiers (such as post-induction treatment and follow-up) on the time-to-event outcomes chosen for the MTC. As such the ERG has limited its appraisal of the methodological quality of the MTC here to a checklist (see Table 3 in the ERG report [see the "Availability of Companion Documents" field]) and brief summary. The checklist shows that some criteria are not met or partially met. Further assessment of the appropriateness of the methods used and of the results and conclusions presented are provided in Appendix 1 in the ERG report.

The MTC uses the four bortezomib-based trials and the MRC MMIX trial which are presented in a network diagram. This shows that there is no closed loop of evidence and as such should not strictly be referred to as an MTC. The creation of a network relies on assumptions (specifically that cyclophosphamide, vincristine, doxorubicin and dexamethasone [CVAD] and VAD are clinically equivalent, and TD and CTD are clinically equivalent) rather than direct evidence through any common comparator. The ERG clinical expert agrees with the assumption, acknowledging the absence of randomised data. As stated in the MS, this, combined with the heterogeneity in the trial designs of bortezomib-based regimens, means that the results of the MTC should be treated with "utmost caution". The manufacturer recognises the limitations of the MTC and results are not used to inform the economic model. The ERG considers the MTC is flawed because: (1) the network is not supported by evidence from trials; (2) it may not be meaningful to generalise over the set of included studies as they may not be sufficiently similar. Therefore, the results may not be reliable. In addition, the limited data available in terms of the number of trials and missing outcomes adds to the unreliability of the results. The ERG agrees with the manufacturer's decision not to use the results of the MTC in the economic model.

See Section 3 in the ERG report for additional information on clinical effectiveness analysis (see the "Availability of Companion Documents" field).

Economic Evaluation

Critical Appraisal of the Manufacturer's Submitted Economic Evaluation

The ERG has considered the methods applied in the economic evaluation in the context of the critical appraisal questions listed in Table 12 in the ERG report, drawn from common checklists for economic evaluation methods.

NICE Reference Case

The NICE reference case requirements have also been considered for critical appraisal of the submitted economic evaluation in Table 13 in the ERG report.

Modelling Approach/Model Structure

A state-transition model was adopted as it allows the clinical pathway of care for transplant-eligible MM patients to be adequately represented. There are distinct phases of treatment and these are captured by the model, from induction prior to stem cell transplant (SCT), SCT, and post-SCT. The model was developed in Microsoft Excel. A schematic is given in Figure 1 in the ERG report.

The MS states that a number of potential model structures were considered but does not state by whom. Model structure and clinical assumptions were discussed at a meeting of the manufacturer's advisory board in October 2012.

Patients enter the model at the start of induction therapy. Post-induction, patients enter one of three health states: complete response (CR), partial response (PR), or non-responders (NR). Some patients may then receive SCT and this is dependent upon their post-induction response. The post-induction response rate also defines the patient's progression-free survival (PFS) and overall survival (OS). Patients move from PFS to second line treatment, then third line treatment, then further line treatment. Patients may move to the death state at any stage. Health-related quality of life (HRQoL) varies by treatment state and in some cases also by the time spent in state.

The model has a lifetime horizon of 30 years in the base case. The model cycle length is one month which reflects the length of a course of treatment with VTD (28 days). Key clinical outcomes used by the model are also reported in months. A half-cycle correction is not used as the cycle length is short relative to the model time horizon.

The model captures the impact of the intervention and differential response to induction therapy with separate health states for CR, PR and NR post-induction, using data from the Pethema trial. Time to progression (TTP) transition probabilities are derived from Pethema trial data1 for each category of response (CR, PR and NR) and by treatment. Transition probabilities to 3rd and further lines of treatment are derived from the APEX trial data which compared bortezomib monotherapy with high dose dexamethasone in patients with relapsed multiple myeloma. Parameter estimates obtained from median survival by response category in the MRC VII trial are used to obtain OS probabilities by post-induction response.

See Section 4 in the ERG report for more information on the cost-effectiveness analysis (see the "Availability of Companion Documents" field).

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Considerations

Technology appraisal recommendations are based on a review of clinical and economic evidence.

Technology Appraisal Process

The National Institute for Health and Care Excellence (NICE) invites 'consultee' and 'commentator' organisations to take part in the appraisal process. Consultee organisations include national groups representing patients and carers, the bodies representing health professionals, and the manufacturers of the technology under review. Consultees are invited to submit evidence during the appraisal and to comment on the appraisal documents.

Commentator organisations include manufacturers of the products with which the technology is being compared, the National Health Service (NHS) Quality Improvement Scotland and research groups working in the area. They can comment on the evidence and other documents but are not asked to submit evidence themselves.

NICE then commissions an independent academic centre to review published evidence on the technology and prepare an 'assessment report'. Consultees and commentators are invited to comment on the report. The assessment report and the comments on it are then drawn together in a document called the evaluation report.

An independent Appraisal Committee then considers the evaluation report. It holds a meeting where it hears direct, spoken evidence from nominated clinical experts, patients and carers. The Committee uses all the evidence to make its first recommendations, in a document called the 'appraisal consultation document' (ACD). NICE sends all the consultees and commentators a copy of this document and posts it on the NICE Web site. Further comments are invited from everyone taking part.

When the Committee meets again it considers any comments submitted on the ACD; then it prepares its final recommendations in a document

called the 'final appraisal determination' (FAD). This is submitted to NICE for approval.

Consultees have a chance to appeal against the final recommendations in the FAD. If there are no appeals, the final recommendations become the basis of the guidance that NICE issues.

Who Is on the Appraisal Committee?

NICE technology appraisal recommendations are prepared by an independent committee. This includes health professionals working in the NHS and people who are familiar with the issues affecting patients and carers. Although the Appraisal Committee seeks the views of organisations representing health professionals, patients, carers, manufacturers and government, its advice is independent of any vested interests.

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

Summary of Appraisal Committee's Key Conclusions

Availability and Nature of Evidence

The Committee was aware that the model only provided comparisons for bortezomib, thalidomide and dexamethasone against thalidomide and dexamethasone and for bortezomib and dexamethasone against vincristine, doxorubicin and dexamethasone, which was not in line with current clinical practice in the United Kingdom (UK), and that the vincristine, doxorubicin and dexamethasone regimen was outside of the scope of this appraisal. The Committee acknowledged that there was no direct evidence available to compare the bortezomib, thalidomide and dexamethasone and the bortezomib and dexamethasone regimens with cyclophosphamide, thalidomide and dexamethasone, and it asked the manufacturer to further explore this by conducting a further indirect comparison using single arms from the relevant clinical trials.

Uncertainties Around and Plausibility of Assumptions and Inputs in the Economic Model

The Committee noted the Evidence Review Group's (ERG) comments that the Medical Research Council (MRC) Myeloma VII trial was not very recent because it recruited patients between 1993 and 2003, and its rates for overall survival and progression-free survival were likely to be lower than would be seen in current clinical practice. The Committee was also aware that although long-term survival end points had not been reached in the PETHEMA and Intergroupe Francophone du Myelome (IFM) trials, the data available in these trials suggested that the manufacturer's model, using data from MRC Myeloma VII, underestimated overall survival.

The Committee concluded that although the impact of stem cell transplant rates included in the model on cost-effectiveness results was uncertain, it was unlikely to undermine the manufacturer's base-case cost-effectiveness results.

Incorporation of Health-related Quality-of-Life Benefits and Utility Values. Have Any Potential Significant and Substantial Health-Related Benefits Been Identified That Were Not Included in the Economic Model, and How Have They Been Considered?

The manufacturer selected the van Agthoven study as the base-case source of utility values because the utility values were obtained using Euro-QoL 5D (EQ-5D).

With regard to adverse events the manufacturer applied a disutility of 0.02 to each patient experiencing an adverse event associated with induction therapy.

The Committee noted the comments from the clinical specialists that the subcutaneous formulation could reduce the risk of peripheral neuropathy and also reduce the need for thromboprophylaxis. The Committee considered that these issues combined might reduce the total cost of bortezomib in the model.

Are There Specific Groups of People for Whom the Technology Is Particularly Cost Effective?

No.

What Are the Key Drivers of Cost-effectiveness?

The manufacturer's deterministic sensitivity analyses highlighted that the results were most sensitive to the mortality for patients who had a complete

response after the induction therapy, and to drug costs.

Most Likely Cost-Effectiveness Estimate (Given as an Incremental Cost-effectiveness Ratio [ICER])

The Committee noted that for bortezomib, thalidomide and dexamethasone compared with thalidomide and dexamethasone, the manufacturer's base-case using the MRC Myeloma VII data as the source for long-term survival ICER resulted in an ICER of £17,800 per quality adjusted life year (QALY) gained.

The Committee was aware that incorporating data from the ERG's preferred Alvares and NMSG 5/94 studies resulted in ICERs of £22,700 and £39,600 per QALY gained respectively.

For bortezomib and dexamethasone compared with cyclophosphamide, thalidomide and dexamethasone, using the MRC Myeloma VII, Alvares and NMSG 5/94 data sources to inform overall survival in the model, the ICERs were £20,600, £24,300 and £33,400 per QALY gained respectively.

The Committee concluded that the ICERs based on survival data from the MRC Myeloma VII and Alvares study were appropriate for its decision making.

Method of Guideline Validation

External Peer Review

Description of Method of Guideline Validation

Consultee organisations from the following groups were invited to comment on the draft scope, Assessment Report and the Appraisal Consultation Document (ACD) and were provided with the opportunity to appeal against the Final Appraisal Determination.

- Manufacturer/sponsors
- Professional/specialist and patient/carer groups
- Commentator organisations (without the right of appeal)

In addition, individuals selected from clinical expert and patient advocate nominations from the professional/specialist and patient/carer groups were also invited to comment on the ACD.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is not specifically stated.

The Appraisal Committee considered clinical and cost-effectiveness evidence submitted by the manufacturer of bortezomib and a review of this submission by the Evidence Review Group (ERG). The main clinical effectiveness evidence came from randomised controlled trials. For cost-effectiveness, the Appraisal Committee considered an economic model submitted by the manufacturer.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate use of bortezomib for induction therapy in multiple myeloma before high-dose chemotherapy and autologous stem cell transplantation

Potential Harms

The Summary of Product Characteristics lists the following as the most commonly reported adverse reactions for bortezomib: nausea, diarrhoea, constipation, vomiting, fatigue, pyrexia, thrombocytopenia, anaemia, neutropenia, peripheral neuropathy (including sensory), headache, paraesthesia, decreased appetite, dyspnoea, rash, herpes zoster and myalgia.

For full details of adverse reactions, see the Summary of Product Characteristics.

Contraindications

Contraindications

For full details of contraindications, see the Summary of Product Characteristics.

Qualifying Statements

Qualifying Statements

- This guidance represents the views of the National Institute for Health and Care Excellence (NICE) and was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.
- Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity and foster good relations. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties.

Implementation of the Guideline

Description of Implementation Strategy

- Section 7(6) of the National Institute for Health and Care Excellence (NICE) (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013 requires clinical commissioning groups, National Health Services (NHS) England and, with respect to their public health functions, local authorities to comply with the recommendations in this appraisal within 3 months of its date of publication.
- When NICE recommends a treatment 'as an option', the NHS must make sure it is available within the period set out in the paragraph above. This means that, if a patient has newly diagnosed multiple myeloma and the doctor responsible for their care thinks that bortezomib is the right treatment, it should be available for use, in line with NICE's recommendations.
- NICE has developed tools (see also the "Availability of Companion Documents" field) to help organisations put this guidance into practice (listed below).
    - Costing template and report to estimate the national and local savings and costs associated with implementation.

Implementation Tools

Mobile Device Resources

Patient Resources

Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

National Institute for Health and Care Excellence. Bortezomib for induction therapy in multiple myeloma before high-dose chemotherapy and autologous stem cell transplantation. London (UK): National Institute for Health and Care Excellence; 2014 Apr. 57 p. (Technology appraisal guidance; no. 311).

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2014 Apr

Guideline Developer(s)

National Institute for Health and Care Excellence (NICE) - National Government Agency [Non-U.S.]

Source(s) of Funding

National Institute for Health and Care Excellence (NICE)

Guideline Committee

Appraisal Committee

Composition of Group That Authored the Guideline

Committee Members: Professor Andrew Stevens (*Chair of Appraisal Committee C*), Professor of Public Health, University of Birmingham; Professor Eugene Milne (*Vice Chair of Appraisal Committee C*), Deputy Regional Director of Public Health, North East Strategic Health

Authority, Newcastle upon Tyne; Dr David Black, Medical Director, NHS South Yorkshire and Bassetlaw; Dr Andrew Burnett, Formerly - Director for Health Improvement and Medical Director, NHS Barnet, London; Gail Coster, Advanced Practice Sonographer, Mid Yorkshire Hospitals NHS Trust; Professor Peter Crome, Honorary Professor, Department of Primary Care and Population Health, University College London; Dr Maria Dyban, General Practitioner, Kings Road Surgery, Cardiff; Dr Greg Fell, Consultant in Public Health, Bradford Metropolitan Borough Council; Dr Peter Jackson, Clinical Pharmacologist, University of Sheffield; Dr Janice Kohler, Senior Lecturer and Consultant in Paediatric Oncology, Southampton University Hospital Trust; Emily Lam, Lay Member; Dr Allyson Lipp, Principal Lecturer, University of South Wales; Dr Grant Maclaine, Formerly - Director, Health Economics & Outcomes Research, BD, Oxford; Dr Andrea Manca, Health Economist and Senior Research Fellow, University of York; Henry Marsh, Consultant Neurosurgeon, St George's Hospital, London; Dr Paul Miller, Director, Payer Evidence, AstraZeneca UK Ltd; Professor Stephen O'Brien, Professor of Haematology, Newcastle University; Dr Anna O'Neill, Deputy Head of Nursing & Healthcare School/Senior Clinical University Teacher, University of Glasgow; Professor Peter Selby, Consultant Physician, Central Manchester University Hospitals NHS Foundation Trust; Professor Matt Stevenson, Technical Director, School of Health and Related Research, University of Sheffield; Dr Tim Stokes, Senior Clinical Lecturer, University of Birmingham; Dr Paul Tappenden, Reader in Health Economic Modelling, School of Health and Related Research, University of Sheffield; Dr Judith Wardle, Lay Member

Financial Disclosures/Conflicts of Interest

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available from the National Institute for Health and Care Excellence (NICE) Web site .

Availability of Companion Documents

The following are available:

- Multiple myeloma – bortezomib (induction therapy). Costing statement. London (UK): National Institute for Health and Care Excellence (NICE); 2014 Apr. 1 p. (Technology appraisal guidance; no. 311). Electronic copies: Available from the National Institute for Health and Care Excellence (NICE) Web site .
- Cooper K, Hartwell D, Copley V, Pickett K, Bryant J. Bortezomib for induction therapy in multiple myeloma before high dose chemotherapy and autologous stem cell transplantation. Southampton (UK): Southampton Health Technology Assessments Centre; 2013. 79 p. Electronic copies: Available in Portable Document Format (PDF) from the NICE Web site .
- Janssen. Single technology appraisal (STA). Specification for manufacturer/sponsor submission of evidence. 2013 Feb. 241 p. Electronic copies: Available in PDF from the NICE Web site .

Patient Resources

The following is available:

- Bortezomib for multiple myeloma before chemotherapy and stem cell transplant. Information for the public. London (UK): National Institute for Health and Care Excellence (NICE); 2014 Apr. (Technology appraisal guidance; no. 311). Electronic copies: Available from the National Institute for Health and Care Excellence (NICE) Web site . Also available for download as an eBook or ePub from the NICE Web site .

publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

This NGC summary was completed by ECRI Institute on June 27, 2014.

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